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Prevention

SINGLE NUCLEOTIDE POLYMORPHISMS IN CHOLESTERYL ESTER TRANSFER PROTEIN (CETP) GENE ARE NOT ASSOCIATED WITH RECURRENT CARDIOVASCULAR EVENTS OR MORTALITY IN PATIENTS WITH ESTABLISHED ATHEROSCLEROSIS: A MENDELIAN RANDOMIZATION EXPERIMENT

Oral Contributions
West, Room 2006
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Background: Although multiple clinical trials using cholesteryl-ester-transfer-protein (CETP) inhibitors are currently enrolling patients with established atherosclerosis, it is not known whether genetic variants affecting CETP are associated with recurrent cardiovascular events (CVE) in these secondary prevention patients.

Methods: Among TexGen registry participants (n = 3717) with established atherosclerosis (those with acute coronary syndrome [ACS] or undergoing coronary artery bypass grafting [CABG]) and available prospective follow-up; we evaluated whether CETP gene variants previously associated with reduced CETP activity and HDL-cholesterol increase (rs708272, rs12149545) are associated with a reduction in recurrent myocardial infarction [MI] (primary outcome), recurrent revascularization, or death (secondary outcomes).

Results: At 4.5 years of follow-up; 439 recurrent MI, 698 recurrent revascularizations, and 756 deaths occured. Using Cox-proportional hazards regression (Table) using additive inheritance model, minor allele for rs708272 and rs12149545 was not associated with primary or secondary outcomes. Results did not change by restricting analyses to whites, analyzing data using dominant inheritance model, or analyzing ACS and CABG groups separately (data not shown).

Conclusions: Genetic CETP variants were not associated with recurrent CVE or mortality. Our results question CETP inhibition as a viable therapeutic target in secondary prevention patients.

Table: Association between single nucleotide polymorphisms affecting CETP levels and the outcome of recurrent myocardial infarction, need for recurrent revascularization, or death

rs708272*		
Genotype (n)	Recurrent MI, n (%)	HR (95% CI)†
GG (1259))	153 (12.2)	Ref
GA (1840)	218 (11.9)	0.95 (0.78-1.17)
AA (618)	68 (11)	0.89 (0.67-1.19)
	Recurrent revascularization, n (%)	HR (95% CI)†
GG (1259)	219 (17.4)	Ref
GA (1840)	363 (19.8)	1.13 (0.95-1.33)
AA (618)	116 (18.8)	1.05 (0.84-1.32)
	Death, n (%)	HR (95% CI)†
GG (1259)	247 (19.6)	Ref
GA (1840)	367 (20)	1.02 (0.86-1.19)
AA (618)	142 (23)	1.11 (0.91-1.37)
rs12149545*		
Genotype (n)	Recurrent MI, n (%)	HR (95% CI)†
GG (1921)	240 (12.5)	Ref
GA (1514)	171 (11.3)	0.88 (0.72-1.07)
AA (282)	28 (9.9)	0.81 (0.55-1.20)
	Recurrent revascularization, n (%)	HR (95% CI)†
GG (1921)	341 (17.8)	Ref
GA (1514)	301 (19.9)	1.10 (0.94-1.29)
AA (282)	56 (19.9)	1.10 (0.83-1.46)
	Death, n (%)	HR (95% CI)†
GG (1921)	380 (19.8)	Ref
GA (1514)	310 (20.5)	1.02 (0.88-1.18)
AA (282)	66 (23.4)	1.13 (0.87-1.47)

* minor allele = A (shown to be associated with reduced CETP activity and increased levels of HDL-C).
†Adjusted for age, gender, hypertension, diabetes, current smoking, renal insufficiency, presence of New York Heart Association Functional Class III/IV symptoms, aspirin use, beta blocker use, and statin use